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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/235,153	01/22/1999	WILFRED A. KELLER	SB-B750	5109
30132	7590	03/25/2003	EXAMINER	
GEORGE A. LOUD 3137 MOUNT VERNON AVENUE ALEXANDRIA, VA 22305			EINSMANN, JULIET CAROLINE	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/235,153	GEORGES ET AL.
Examiner	Art Unit	
Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 18 December 2002 and 30 December 2002.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 91-98 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) 83-85 is/are allowed.

6) Claim(s) 81-82, 86-91 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 22 January 1999 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. ____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____ .
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6) Other: _____

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 12/18/02 and 12/30/02. Claims 34-38, 40-46, and 48-80 have been canceled. Claims 81-98 were added. Claims 81-98 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. This action is **FINAL**.

Claim Rejections - 35 USC § 112

2. Claims 81-82, 86-98 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen* , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "said enzyme not naturally occurring in said secondary metabolic pathway" or "said enzyme not naturally occurring in said phenylpropanoid pathway" or in claims 81, 82, and 89 appears to represent new matter. Applicant argues that support for this amendment can be found throughout the specification, referring particularly to examples 1-6, which describe the use of choline oxidase to modify the utilization of an intermediate substrate in the phenylpropanoid secondary metabolic pathway.

Further, applicant suggests that broad support is found at page 31 wherein it is explained that the term “heterologous” refers to an enzyme not normally associated with phytate biosynthesis.

However, these portions of the specification are not sufficient to provide support for the broad negative limitation that excludes any enzyme that is not naturally occurring a secondary metabolic pathway. Applicant’s narrow definition of heterologous in the specification (“By heterologous it is meant an enzyme not normally associated with phytate biosynthesis in said plant cell (p. 31, lines 10-12)” is not a generalization which applies to any heterologous gene used in the specification. Within the art, a “heterologous gene” is understood to be “any gene that is isolated from organism A and transferred into organism B” (Dictionary of Gene Technology, 1995, p. 210). However, Applicant’s arguments seem to be implying that a protein that is “not naturally occurring in the secondary metabolic pathway” to the pathway has some narrower definition wherein the protein must not be active in the corresponding metabolic pathway in different plant species, for example. That is, applicant appears to be arguing that “not naturally occurring in the secondary metabolic pathway” is narrower than “heterologous,” but this is not clear from the specification. No specific basis for this definition was identified in applicant’s paper, nor did a review of the specification by the examiner find any basis for the limitation. It is this narrower definition of “not naturally occurring in the secondary metabolic pathway” that is not supported by the specification. As noted by MPEP 2173.05(i),

“Any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983) aff’d mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement.”

Since no basis has been identified, the claims are rejected as incorporating new matter.

Claim Rejections - 35 USC § 102

3. Claims 81, 86, 87, 88, 89, 94, 95, 98 rejected under 35 U.S.C. 102(e) as being anticipated by Cheng *et al.* (US 5948667).

Cheng *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of an intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant, said enzyme not naturally occurring in said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence operably linked to a seed-specific promoter, said plant being *B. napus* (canola);

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Col. 17, line 56-Col. 19, line 25).

The methods taught by Cheng *et al.* comprise the transformation of *B. napus* with an expression vector comprising a seed specific promoter (the oleosin promoter) and a coding sequence for xylanase. The transformation of the plant with a coding sequence xylanase results in the production of transgenic plants with altered nutritional profiles because they contain a higher level of xylanase than wild type plants.

The selection step undertaken by Cheng *et al.* was to select the enzyme xylanase for its ability to modify hemicellulose levels in plants. Xylanase is inherently a protein capable of

modifying the utilization of an intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant, and thus, Cheng *et al.* have made a selection as required by the first step of the claim.

Claim Rejections - 35 USC § 103

4. Claims 81, 82, 86, 87, 88, 89, 90, 94, 95, 96, 97, and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murata in view of Willmitzer *et al.* (WO 92/01042).

Murata teaches a method of making a genetically transformed plant comprising: selecting a nucleic acid sequence for its ability to encode a protein capable of modifying the utilization of an intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant, said enzyme not naturally occurring in said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence operably linked to a promoter; recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (see Examples 8 (page 8) and 14 (page 10)).

The methods taught by Murata are specifically directed for the purpose of producing osmo-tolerant plants, however, these methods necessarily meet the limitations of the instant claims. Murata specifically selects a gene encoding choline oxidase for plant transformation, selecting the choline oxidase for its ability to encode choline oxidase, a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway. Thus, Murata has

selected a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant. The transgenic plants recovered by Murata inherently have an altered nutritional profile by virtue of the fact that they are expressing choline oxidase. These plants would have lower lignin and sinapine content.

Murata further grows the plant obtained under conditions which permit the formation of a seed (page 10, line 10, for example). Murata teaches the plants and seeds produced by the plants obtained by this method (page 10, line 10-15), these seeds inherently have reduced lignin and sinapine content.

Murata exemplifies the use of this method to produce transgenic *Arabidopsis thaliana*, of the family cruciferae, (example 8) and rice, *Oryza sativa*- family gramineacae (example 10).

Murata further teaches that choline oxidase is an enzyme which is commercially available (p. 2, lines 55-56).

Murata does not teach methods in which the promoter is tissue selective, or specifically seed selective, and Murata does not teach plants that are selected from the group consisting of corn, canola, wheat, barley, oats, alfalfa, soybeans and sorghum.

Willmitzer *et al.* teach transgenic plants expressing industrial enzymes, and methods for the production of such plants. The industrial enzymes suggested by Willmitzer *et al.* for use in these methods include oxidoreductases (p. 6, line 22). They teach that the DNA sequence encoding the enzyme of interest under the control of a promoter such as a seed specific promoter such as the phaseolin promoter (p. 4, lines 27-31). Willmitzer *et al.* teach a variety of plants useful for the introduction of the enzyme, including tobacco, potato, tomato, pea, soy, and

cereals (p. 7, lines 19-21), and further teach that either the entire plant or parts thereof may be useful for animal feeds (p. 7, lines 10-13). Willmitzer *et al.* teach vectors for the integration of foreign DNA into plant cells and the introduction of these vectors into *Agrobacterium* species (p. 9, line 28-p. 9, line 19).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used seed specific promoters for the expression of choline oxidase in plants as taught by Willmitzer *et al.* The ordinary practitioner would have been motivated to do so by the fact that choline oxidase is an enzyme which is sold commercially and because Willmitzer *et al.* expressly teach that the production of enzymes in plants overcomes two major obstacles in industrial enzyme production, “Firstly, higher plants have biosynthetic capacity to perform the requisite post-translational modifications occurring in eukaryotic cells of mammalian or other origin. Secondly, transgenic plants grown in the field need very little extra energy for growth (and hence for the production of proteins such as industrial enzymes) and furthermore do not give rise to any major problems with respect to waste management (p. 4, lines 10-18).” Furthermore, Murata provides the nucleic acid sequence encoding choline oxidase and demonstrates that it can be successfully expressed in transgenic plants. Willmitzer *et al.* provide the necessary suggestion and direction to motivate the production of choline oxidases in plants, and the claimed invention is obvious over the prior art.

5. Claims 81, 82, 86, 87, 88, 89, 90, 94, 95, 96, 97, and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapple *et al.* (WO 97/23599) in view of both Kennley (WO 5662958) and Willmitzer *et al.* (WO 92/01042).

Chapple *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of an intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant, said enzyme not naturally occurring in said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence operably linked to a promoter;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Example 5).

Chapple *et al.* teach the transformation of plants with the F5H gene in order to alter the lignin content in plants. Chapple *et al.* exemplify this method in the transformation of *Arabidopsis thaliana* (a crucifer) and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (*Brassica*) (p. 7, lines 15-20). Chapple *et al.* teach the growth of such plants to permit the formation of seed, and the recovery of said seed (p. 19, lines 4-5). Chapple *et al.* teach the use of tissue specific promoters (p. 15, lines 25-29).

Chapple *et al.* teach method steps in which at least one genetically altered plant having altered lignin content is identified (p. 24 line 25-p. 24 line 7, Tables 1 and 2). Since the F5H gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine, (i.e. 5-hydroxyferulic acid) plants with decreased F5H activity as taught by Chapple *et al.* would inherently have the property of decreased sinapine levels compared to the wild type plants.

Chapple *et al.* do not teach methods in which a seed selective promoter is used to direct the expression of the nucleic acid sequence to seeds.

At the time the invention was made, it was routine to use the seeds of cruciferous plants as animal feed. Furthermore, it was widely known that the lignin content in such seeds is an anti-nutritional factor. For example, Kennley *et al.* teach that lignin within canola seed prevents extensive degradation of cellulose and hemicellulose by cellulolytic microorganisms (Col. 3, lines 30-40).

Willmitzer *et al.* provide methods for the transformation of plants with heterologous polypeptides, and specifically teach methodology for the direction of such heterologous polypeptides to the seeds of such plants. They teach that the DNA sequence encoding the enzyme of interest under the control of a promoter such as a seed specific promoter such as the phaseolin promoter (p. 4, lines 27-31).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used seed specific promoters such as those provided by Willmitzer *et al.* in the methods taught by Chapple *et al.* The ordinary practitioner would have been motivated to produce such plants in order to provide canola seed (*Brassica napus*) which has reduced lignin content, since Kennley *et al.* teach that “lignin within the canola seed coat prevent extensive degradation of cellulose and hemicellulose by cellulolytic microorganisms in the rumen or by the acidic environment of the abomasum and the small intestine. Some method of treatment is required to alter the seed to a form suitable for utilization by ruminants (Col. 3, lines 33-37).” Thus, in light of the teachings provided in the prior art, the instant invention is obvious to one of ordinary skill in the art at the time the invention was made.

6. Claims 82, 86, 87, 88, 89, 90, 94, 95, 96, 97, and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorsselaere *et al.* (WO 93/05160) in view of both Kennley (WO 5662958) and Willmitzer *et al.* (WO 92/01042).

Van Doorsselaere *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant, said protein being non-native to said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Example 4).

Van Doorsselaere *et al.* teach the transformation of plants with a nucleic acid encoding O-methyl transferase (OMT) in order to alter the lignin content in plants. Van Doorsselaere *et al.* exemplify this method in the transformation of poplar trees and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (*Brassica*) (p. 13, lines 15-26). Van Doorsselaere *et al.* teach the use of tissue specific promoters (p. 12, lines 15-20). Van Doorsselaere *et al.* teach method steps in which at least one genetically altered plant having altered lignin content is identified (p. 21 -23). Since the OMT gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine, (i.e. ferulic acid) plants with decreased OMT activity as taught by Van Doorsselaere *et al.* would inherently have the property of decreased sinapine levels compared to the wild type plants.

Van Doorselaere *et al.* do not teach methods in which a seed selective promoter is used to direct the expression of the nucleic acid sequence to seeds.

At the time the invention was made, it was routine to use the seeds of cruciferous plants as animal feed. Furthermore, it was widely known that the lignin content in such seeds is an anti-nutritional factor. For example, Kennley *et al.* teach that lignin within canola seed prevents extensive degradation of cellulose and hemicellulose by cellulolytic microorganisms (Col. 3, lines 30-40).

Willmitzer *et al.* provide methods for the transformation of plants with heterologous polypeptides, and specifically teach methodology for the direction of such heterologous polypeptides to the seeds of such plants. They teach that the DNA sequence encoding the enzyme of interest under the control of a promoter such as a seed specific promoter such as the phaseolin promoter (p. 4, lines 27-31).

Therefore, It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used seed specific promoters such as those provided by Willmitzer *et al.* in the methods taught by Van Doorselaere *et al.* The ordinary practitioner would have been motivated to produce such plants in order to provide canola seed (*Brassica napus*) which has reduced lignin content, since Kennley *et al.* teach that “lignin within the canola seed coat prevent extensive degradation of cellulose and hemicellulose by cellulolytic microorganisms in the rumen or by the acidic environment of the abomasum and the small intestine. Some method of treatment is required to alter the seed to a form suitable for utilization by ruminants (Col. 3, lines 33-37).” Thus, in light of the teachings provided in the prior art, the instant invention is obvious to one of ordinary skill in the art at the time the invention was made.

RESPONSE TO REMARKS

Applicant's remarks are addressed insofar as they are relevant to the rejections of the instantly pending claims.

Applicant submits that Cheng *et al.* do not teach or suggest the limitations reciting "selecting a nucleic acid sequence for its ability to encode an enzyme capable of modifying the utilization of an intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant, said enzyme not naturally occurring in said secondary metabolic pathway (response p. 9)," because Cheng *et al.* fail to teach that the enzymatic activity of recombinant xylanase acts upon any intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant. This is not persuasive because the selection step undertaken by Cheng *et al.* was to select the enzyme xylanase for its ability to modify hemicellulose levels in plants. Xylanase is inherently a protein capable of modifying the utilization of an intermediate substrate in a secondary metabolic pathway associated with a nutritional profile in a plant (whether or not Cheng *et al.* mention that hemicellulose is also a substrate in a secondary metabolic pathway), and thus, Cheng *et al.* have made a selection as required by the first step of the claim.

Applicant further suggests that the examiner has not established that the xylanase enzyme used by Cheng *et al.* is not naturally occurring in metabolic pathways that use hemicelluloses as a substrate. However, this is not persuasive. Applicant's interpretation of the limitation "not naturally occurring" appears to be different from the examiner's. In this case, "not naturally occurring in the metabolic pathway" is understood to mean that the particular enzyme being expressed by the expression construct is not naturally present in the metabolic pathway of the

plant host. The xylanase being used in the methods taught by Cheng *et al.* was originally isolated from a fungal species, and therefore, it is clearly not naturally occurring in any metabolic pathway of the plants transformed by Cheng *et al.* This interpretation of “not naturally occurring” is within the broadest reasonable interpretation of the claims (Col. 5, lines 27-29). Applicant further submits that Cheng *et al.* teaches that in the methods taught by Cheng *et al.* the xylanase would not be available to modify an intermediate in a secondary metabolic pathway of a plant until after the plant is harvested. However, the claims contain no requirement that the modification of any substrates by the enzyme occur prior to harvesting the plants. Thus, this argument is not persuasive.

The 102 rejections in view of Chapple *et al.* and Van Doorsselaere *et al.* are withdrawn because they do not teach every limitation of the instant claims (see 103 rejections set forth herein). The rejection of Murata *et al.* in view of Londenborough *et al.* is withdrawn in view of applicant’s amendment to the claims requiring a seed-specific promoter.

Applicant argues that the rejection over Murata *et al.* in view of Willmitzer *et al.* should be withdrawn because there is no motivation to combine the two references and because the combination would be unworkable. However, this is not persuasive. In this rejection, Murata *et al.* is relied upon for their teaching of the methodology for the expression of choline oxidase in transgenic plants. Although Murata *et al.*’s purpose for completing such a method is different than the motivation provided in the rejection, nonetheless, Murata *et al.* provide a method for transforming plants with an industrial enzyme. Murata *et al.* specifically teach that choline oxidase is an industrial enzyme. The teachings of Willmitzer *et al.* provide an alternate use for the methods of Murata *et al.* and provide a motivation to modify the method for transforming

plants with choline oxidase, as discussed in the rejection above. The transformation of plants with choline oxidase using a seed-specific promoter provides a new use for methods which utilize plants transformed with choline oxidase as taught by Murata *et al.* Thus, this rejection is also maintained.

Applicant's further argues that the mere fact that the teachings of Willmitzer *et al.* and Murata *et al.* can be combined does not render the combination obvious because there is nothing in Willmitzer *et al.* or Murata *et al.* to suggest the unexpected result of reduced sinapine when the plants are transformed with choline oxidase. This argument is persuasive with regard to claims 83, 84, 85, 91, 92, and 93 which are commensurate in scope with the unexpected result. The remaining rejected claims are generic in nature, and generically, it is obvious to transform plants using the combined guidance provided in the references of Murata *et al.* in view of Willmitzer *et al.* to produce choline oxidase in plants, for all of the reasons of record. The MPEP states that "the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range (MPEP 716.02(d))." In the instant case, the rejected claims are not commensurate in scope with the demonstrated unexpected results.

Applicant argues that Murata *et al.* are not concerned with altering the nutritional profile of the plant. However, as previously stated, the alteration of the nutritional profile of the plant when transforming it with a gene encoding choline oxidase is a necessary effect of such a transformation. Murata *et al.* completes such a transformation, and thus changes the nutritional profile of a plant whether they were aware of this feature of their method or not. Applicant further argues that Willmitzer *et al.* are very clear that it is not their purpose to change the physical characteristics of the plant itself, citing language from Willmitzer *et al.* that notes that

their invention comprises transgenic plants transformed with nucleic acids encoding enzymes “with the exception of enzymes conferring improved growth properties or desirable physical characteristics to living plants producing them.” However, Willmitzer *et al.* further state that “the enzyme will typically not confer improved growth properties (e.g. increased resistance against pests or pathogens), a higher content of nutrients (by means of an altered amino acid composition) or desirable physical characteristics (i.e. reduced viscosity of fruit products) to a plant (*if it does, this will be incidental to the true purpose which is to synthesize the enzyme*) (emphasis added) (p. 3, lines 14-21).” Thus, Willmitzer *et al.* are not teaching away from plants with desirable physical characteristics, they are simply not transforming plants with these effects as the goal. Applicant is reminded that MPEP 2123 teaches that “A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments.” Thus, simply because Willmitzer *et al.* have a different purpose than applicant, does not mean that they teach away from the instantly claimed invention. The rejection is quite clear in providing that the motivation for production of transgenic plants expressing a heterologous nucleic acid that encodes choline oxidase is to provide a means for the production of this industrially useful enzyme. Thus, the examiner concludes that Willmitzer *et al.* do not teach away from the claimed invention, and the rejection of record is maintained for claims that are not commensurate in scope with the demonstrated unexpected results.

With regard to the rejection in view of Chapple *et al.* in view of Kennley *et al.* and Willmitzer *et al.*, applicant argues that none of these references teach that the enzyme expressed by the transgene does not naturally occur in the secondary metabolic pathway in which the utilization of an intermediate substrate is to be modified because F5H is an enzyme within the

portion of the phenylpropanoid metabolic pathway that relates to lignin synthesis. However this is not persuasive. Again, applicant's interpretation of the limitation "not naturally occurring" appears to be different from the examiner's. In this case, "not naturally occurring in the metabolic pathway" is understood to mean that the particular enzyme being expressed by the expression construct is not naturally present in the metabolic pathway of the plant host. The FH5 gene being used by Chapple *et al.* is from Arabidopsis, and they teach the transformation of a wide variety of plant species with this gene. In the cases wherein the Arabidopsis gene would be transformed into any other plant species other than Arabidopsis (for example, corn) then the expressed Arabidopsis protein would not be naturally occurring in the pathway of the corn plant, even if the corn plant expresses an enzyme with similar function. The enzymes themselves are proteins themselves are different. This interpretation is supported by the fact that applicant cites the use of the word "heterologous" as support for the addition of this limitation to the claims. A "heterologous gene" is understood to be "any gene that is isolated from organism A and transferred into organism B" (Dictionary of Gene Technology, 1995, p. 210). Chapple *et al.* specifically teach that their method "relates to the modification of lignin composition in a plant cell by the introduction of a foreign plant gene encoding an active ferulate-5-hydroxylase (F5H) enzyme (p. 1, lines 7-9)." Thus, the enzyme being introduced into the plants is a non-native enzyme, in the sense that it is not the enzyme that is naturally encoded by the transgenic plants, even if it has the same function as an enzyme that may be functional in that pathway. Thus, the rejection which utilizes Chapple *et al.* is maintained.

Applicant sets forth a similar position in an attempt to overcome rejections in view of Van Doorselaere *et al.* However, these are not persuasive for the same reason that the argument

is not persuasive in view of the Chapple *et al.* reference. Applicant's interpretation of the claim is apparently narrower than the examiner's. However, as discussed by the examiner, the examiner's interpretation is within the broadest reasonable interpretation of the claims.

Allowable Subject Matter

7. Claims 83, 84, 85, 91, 92, and 93 are free of the prior art. Thus, claims 83, 84, and 85 are allowed since they are not rejected herein under any statute. Claims 91, 92, and 93 are rejected as containing new matter but are drawn to subject matter that is free of the prior art.

8. While the prior art teaches methods for producing transgenic plants expressing heterologous choline oxidase (Murata, for example) and different transgenic plants expressing betaine aldehyde dehydrogenase (Holmström *et al.*, for example), the prior art does not teach or suggest methods in which both choline oxidase and betaine aldehyde dehydrogenase are introduced into the same plant under the control of a seed specific promoter. Further, the unexpected results provided in the specification and referred to by Applicant in the arguments overcome the rejections in view of Murata *et al.* and Willmitzer *et al.* for the claims that are limited to the scope of the unexpected results.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C Einsmann
Examiner
Art Unit 1634

March 21, 2003